

English Translation of the International Application as filed

(35 U.S.C. 371(c)(2))

### Description

#### ~~Photosensitive Resin Composition and~~ Method for Forming Hydrogel

#### Technical Field

The present invention relates to a photopolymerizable photosensitive resin composition and to a method for forming a hydrogel from the composition.

#### Background Art

Poly((meth)acrylic acid) and an alkali-neutralized product thereof are highly miscible with hydrophilic physiologically active substances such as drug ingredients and enzymes. Thus, for the purpose of retaining and immobilizing hydrophilic substances, such polymers are employed in wastewater treatment and as a base material for a diagnostic drug, a cataplasm, etc. In most cases, such a base material is hardened under hydrous conditions through cross-linking so as to retain and immobilize a substance of interest. The thus-hardened product is generally called "hydrogel." Water plays important roles in hydrogel, including dissolving a substance in a film-form substrate, controlling rate of releasing a substance to the outside, and

controlling rate of mass diffusion from the outside.

Conventionally, hydrogel of poly((meth)acrylic acid) or an alkali-neutralized product thereof is formed through hardening by heat. When a substance having poor thermal stability or a volatile substance is immobilized in gel, the polymer must be hardened at low temperature. Thus, completion of gel formation and immobilization requires a very long period of time (e.g., several days), which is problematic (Japanese Patent Application Laid-Open (*kokai*) No. 5-320612).

In recent years, a non-thermal method, employing a photocurable resin, for immobilizing a thermally instable physiologically active substance such as an enzyme or bacterial cells has become known as an advantageous method in the art (Japanese Patent Publication (*kokoku*) No. 8-23545, and Japanese Patent Application Laid-Open (*kokai*) Nos. 2-240555 and 2-308805).

Among photosensitive resins disclosed in the above documents, so-called PVA-SbQ resin has drawbacks. Specifically, since PVA-SbQ resin has a cationic moiety in the molecule, only limited compounds may be dissolvable or miscible in immobilization of a physiologically active substance, an enzyme, or bacterial cells. In addition, in the presence of a large amount of water, photosensitivity of PVA-SbQ resin decreases considerably. Thus, when a compound that cannot be subjected to a drying step is immobilized under hydrous conditions, the formed gel has poor strength,

due to insufficient hardenability.

Another photopolymerizable composition, which is a composition containing a cellulose-based polymer, has poor photosensitivity. When such a composition is used, an additional polymerizable monomer is required to be incorporated into the composition so as to attain sufficient hardenability. However, complete polymerization of the polymerizable monomer through photocuring reaction is virtually impossible, and the remaining unreacted monomer problematically inhibits enzymatic activity or causes skin irritation. Thus, the cellulose-based polymer composition is difficult to employ for immobilizing enzymes or producing a cataplast.

Conventionally, there has known a technique for introducing a polymerizable cross-linking moiety into poly((meth)acrylic acid) by use of a (meth)acrylate ester having an epoxy group (Japanese Patent Application Laid-Open (*kokai*) No. 49-98878). However, the document does not disclose a photocurable and water-containing composition, and the disclosed approach polymer cannot be employed for the formation of a hydrogel, which is an object to be attained by the present inventors.

Similarly, there have been reported some techniques for introducing a cross-linking group into a poly((meth)acrylic acid) copolymer by use of a (meth)acrylate ester having an epoxy group (Japanese Patent Application Laid-Open (*kokai*) Nos. 10-3167 and 4-337087). Although the above copolymers

are photocurable, the copolymers are provided for use in photoresist and have a pH-dependent water-solubility; i.e., have poor solubility in water under weak acidic to neutral conditions. Thus, the copolymers exhibits insufficient physical properties, including miscibility with other compounds and water content of gel during the formation of a hydrogel, which is an object to be attained by the present inventors.

As described above, poly((meth)acrylic acid) is a key compound for formation of hydrogel for use in a cataplasm, a diagnostic drug, or wastewater treatment, and photocuring is an effective technique for forming a hydrogel for the above uses. However, there have never been developed a useful technique employing poly((meth)acrylic acid) and photocuring in combination.

#### Disclosure of the Invention

In view of the foregoing, an object of the present invention is to provide a photosensitive resin composition formed from poly((meth)acrylic acid), which composition exhibits excellent storage stability, affinity, miscibility, or solubility with respect to a variety of compounds, and high sensitivity, and allows these compounds to be photo-immobilized even under hydrous conditions. Another object of the invention is to provide a method for forming a hydrogel from the composition.

Meanwhile, in recent years, there have been reported

cross-linkable polymers and oligomers which have been synthesized from an acrylate ester having an epoxy group and into which an alkylene group serving as a spacer has been introduced between an epoxy group and an acryl group (Japanese Patent Application Laid-Open (*kokai*) Nos. 11-327139 and 2001-58972). In these polymers and oligomers, due to the spacer effect of the alkylene group, a (meth)acryl group comes to have a higher degree of freedom. Thus, the polymers and oligomers are excellent materials in terms of enhanced rate of reaction, improved physical properties of cured products (e.g., toughness of cured products) and advantageous safety (e.g., reduced toxicity and irritation). However, these documents disclose neither a water-soluble composition nor a water-containing composition, and disclose that the polymers and oligomers are not water-soluble. According to the above reported polymers and oligomers, formation of a hydrogel which is to be attained by the present inventors cannot be attained.

In order to attain the aforementioned objects, the present inventors have carried out extensive studies, and have found that, through use of a poly((meth)acrylic acid)-based water-soluble photo-sensitive resin formed of a ((meth)acrylic acid)-based polymer in which a compound represented by formula (1) has been added to portions of the carboxylic groups, there can be produced a photosensitive resin composition which exhibits excellent storage stability, affinity, miscibility, or solubility with respect to a



polymer to which the compound represented by formula (1) has not been added are partially or entirely neutralized with an alkali.

A third mode of the present invention provides a method for forming a hydrogel characterized by comprising subjecting a photosensitive resin composition of the first or second mode to photopolymerization.

#### Best Modes for Carrying Out the Invention

The photosensitive resin composition of the present invention contains a poly((meth)acrylic acid)-based water-soluble photo-sensitive resin (A), a photopolymerization initiator (B), and water (C).

The photosensitive resin (A) may be produced through epoxy-ring-opening addition of a compound represented by formula (1) to portions of the carboxylic groups present in a ((meth)acrylic acid)-based polymer.

Examples of the compound represented by formula (1) include 2-hydroxyethyl acrylate glycidyl ether, 2-hydroxyethyl methacrylate glycidyl ether, 2-hydroxypropyl acrylate glycidyl ether, 2-hydroxypropyl methacrylate glycidyl ether, 4-hydroxybutyl acrylate glycidyl ether, and 4-hydroxybutyl methacrylate glycidyl ether.

The poly((meth)acrylic acid)-based polymer may be a (meth)acrylic acid homopolymer or a copolymer of two or more monomers selected from among (meth)acrylic acid monomer, a vinyl monomer, and a (meth)acrylate monomer. The

poly((meth)acrylic acid)-based polymer may be a side-chain-modified product with a compound other than the compound represented by formula (1). In any case, the poly((meth)acrylic acid)-based polymer is selected such that the polymer to which the compound represented by formula (1) has been added has an acid value of 150 mgKOH/g or more on a solid basis, preferably 170 mgKOH/g or more.

No particular limitation is imposed on the molecular weight of the photosensitive resin (A), and the weight average molecular weight is preferably 5,000 to 2,000,000. When the molecular weight is less than 5,000, hardenability may be poor, whereas when the molecular weight is in excess of 2,000,000, viscosity of the resin excessively increases, causing difficulty in synthesis and in application of the resin composition to a substrate.

No particular limitation is imposed on the percent addition of the compound represented by formula (1), and the percent addition is determined in accordance with cross-linking density and mechanical strength of a hardened product of interest. In any case, the percent addition is controlled such that the photosensitive resin (A) after addition has an acid value of 150 mgKOH/g or more on a solid basis, preferably 170 mgKOH/g or more. When the acid value is less than 150 mgKOH/g, sufficient water solubility fails to be attained.

The addition reaction of the compound represented by formula (1) to portions of the carboxylic groups present in a



((meth)acrylic acid)-based polymer, thereby forming the photosensitive resin (A), is generally carried out in a solution with heating and/or in the presence of a catalyst. No particular limitation is imposed on the solvent forming the solution, and the solvent preferably has a composition for dissolving the poly((meth)acrylic acid)-based polymer employed. Examples of the solvent include water; methanol; ethanol; 2-propanol; n-butanol; sec-butanol; isobutanol; tert-butanol; ethylene glycols such as ethylene glycol, diethylene glycol, triethylene glycol, and tetraethylene glycol; glycol ethers such as ethylene glycol monomethyl ether, diethylene glycol monomethyl ether, ethylene glycol diethyl ether, and diethylene glycol dimethyl ether; glycol ether acetates such as ethylene glycol monoethyl ether acetate, diethylene glycol monoethyl ether acetate, and diethylene glycol monobutyl ether acetate; propylene glycols such as propylene glycol, dipropylene glycol, and tripropylene glycol; propylene glycol ethers such as propylene glycol monomethyl ether, propylene glycol monoethyl ether, dipropylene glycol monomethyl ether, dipropylene glycol monoethyl ether, propylene glycol dimethyl ether, dipropylene glycol dimethyl ether, propylene glycol diethyl ether, and dipropylene glycol diethyl ether; propylene glycol ether acetates such as propylene glycol monomethyl ether acetate, propylene glycol monoethyl ether acetate, dipropylene glycol monomethyl ether acetate, and dipropylene glycol monoethyl ether acetate; dimethylsulfoxide; N-

methylpyrrolidone; dimethylformamide; dimethylacetamide; and mixture thereof.

No particular limitation is imposed on the catalyst used in the reaction. Examples of acid catalysts include inorganic acids such as sulfuric acid, phosphoric acid, perchloric acid; Lewis acids such as  $\text{BF}_3$ ; and organic sulfonic acids such as methanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, and dodecylbenzenesulfonic acid. Examples of basic catalysts include tertiary amines such as triethylamine, tetramethylethylenediamine, tributylamine, tri-n-octylamine, dimethylbenzylamine, and pyridine; quaternary ammonium salts such as tetramethylammonium chloride, tetramethylammonium bromide, tetraethylammonium bromide, and tetrabutylammonium bromide; and phosphorus compounds such as triphenylphosphine and tributylphosphine.

No particular limitation is imposed on the reaction temperature. Generally, the reaction is preferably performed at room temperature to 120°C.

When the photosensitive resin composition of the present invention is produced from a photosensitive resin that has been synthesized with a solvent other than water, the synthesized photosensitive resin may be simply diluted with water. Alternatively, there may be employed distillation and substitution of the solvent; drying to solid and dissolving the solid in water; or pouring the resin into a non-polar solvent such as aliphatic hydrocarbon, aromatic hydrocarbon, ethyl acetate, or butyl acetate, separating the

precipitated solid, and re-dissolving the solid in water.

Notably, the carboxylic groups remaining in the photosensitive resin (A) may be free-acid form or alkali-neutralized form. No particular limitation is imposed on the alkali compound, and examples of employable alkalis include inorganic alkalis such as lithium, sodium, and potassium; ammonia; primary to tertiary alkylamines; and quaternary ammonium compounds. No particular limitation is imposed on the neutralization degree, and neutralization may be appropriately regulated so as to attain a pH suited for the purpose of use.

No particular limitation is imposed on the solid content of the photosensitive resin composition of the present invention containing the photosensitive resin (A), a photopolymerization initiator (B), and water, and the solid content is, for example, 3% to 50%. When the solid content falls within the range, a particularly strong gel can be formed.

The photosensitive resin composition of the present invention essentially contains a photopolymerization initiator and may further contain a photosensitizer. Upon incorporation of the photopolymerization initiator into the composition, the initiator may be dissolved or dispersed in the composition. Alternatively, the initiator may be chemically linked to the photosensitive resin. When the photopolymerization initiator is dissolved or dispersed in the composition, the photopolymerization initiator is

generally incorporated in an amount of 0.1 to 30 wt.% with respect to the amount of the photosensitive resin, preferably 1 to 10 wt.%. No particular limitation is imposed on the photopolymerization initiator and photosensitizer employed in the composition. Examples include benzophenones such as benzophenone, hydroxybenzophenone, bis-N,N-dimethylaminobenzophenone, bis-N,N-diethylaminobenzophenone, and 4-methoxy-4'-dimethylaminobenzophenone; thioxanthenes such as thioxanthone, 2,4-diethylthioxanthone, isopropylthioxanthone, chlorothioxanthone, and isopropoxychlorothioxanthone; anthraquinones such as ethylanthraquinone, benzanthraquinone, aminoanthraquinone, and chloroanthraquinone; acetophenones; benzoin ethers such as benzoin methyl ether, benzoin ethyl ether, and benzoin phenyl ether; 2,4,6-trihalomethyltriazines; 1-hydroxycyclohexyl phenyl ketone; 2,4,5-triarylimidazole dimers such as 2-(o-chlorophenyl)-4,5-diphenylimidazole dimer, 2-(o-chlorophenyl)-4,5-di(m-methoxyphenyl)imidazole dimer, 2-(o-fluorophenyl)-4,5-diphenylimidazole dimer, 2-(o-methoxyphenyl)-4,5-diphenylimidazole dimer, 2-(p-methoxyphenyl)-4,5-diphenylimidazole dimer, 2,4-di(p-methoxyphenyl)-5-phenylimidazole dimer, and 2-(2,4-dimethoxyphenyl)-4,5-diphenylimidazole dimer; benzyl dimethyl ketal; 2-benzyl-2-dimethylamino-1-(4-morpholinophenyl)-butan-1-one; 2-methyl-1-[4-(methylthio)phenyl]-2-morpholino-1-propanone; 2-hydroxy-2-methyl-1-phenyl-propan-1-one; 1-[4-(2-hydroxyethoxy)-phenyl]-2-hydroxy-2-methyl-1-propan-1-one;

phenanthrenequinone; 9,10-phenanthrenequinone; benzoin such as methylbenzoin and ethylbenzoin; acridine derivatives such as 9-phenylacridine and 1,7-bis(9,9'-acridinyl)heptane; bisacylphosphine oxide; and mixture thereof.

In addition to the above initiators, other additives such as a promoter may also be added. Examples of the promoter include ethyl p-dimethylaminobenzoate, isoamyl p-dimethylaminobenzoate, ethanolamine, diethanolamine, and triethanolamine.

To the photosensitive resin composition of the present invention, a polymerizable monomer may be added in order to regulate sensitivity of the composition and physical properties of the hardened products. Examples of the monomer include polyethylene glycol diacrylate (No. of ethylene oxide unit: 2 to 14), polyethylene glycol dimethacrylate (No. of ethylene oxide unit: 2 to 14), trimethylolpropane diacrylate, trimethylolpropane dimethacrylate, trimethylolpropane triacrylate, trimethylolpropane trimethacrylate, trimethylolpropane ethoxytriacylate, trimethylolpropane ethoxytrimethacrylate, trimethylolpropane propoxytriacylate, trimethylolpropane propoxytrimethacrylate, tetramethylolmethane triacylate, tetramethylolmethane trimethacrylate, tetramethylolmethane tetraacylate, tetramethylolmethane tetramethacrylate, polypropylene glycol diacrylate (No. of propylene oxide unit: 2 to 14), polypropylene glycol dimethacrylate (No. of propylene oxide unit: 2 to 14), dipentaerythritol pentaacylate,

dipentaerythritol pentamethacrylate, dipentaerythritol hexaacrylate, dipentaerythritol hexamethacrylate, bisphenol A polyoxyethylene diacrylate, bisphenol A polyoxyethylene dimethacrylate, bisphenol A dioxyethylene diacrylate, bisphenol A dioxyethylene dimethacrylate, bisphenol A trioxyethylene diacrylate, bisphenol A trioxyethylene dimethacrylate, bisphenol A decaoxyethylene diacrylate, bisphenol A decaoxyethylene dimethacrylate, esterified products of polyhydric carboxylic acid (e.g., phthalic anhydride) and a compound having a hydroxyl group and an ethylenic unsaturated group (e.g.,  $\beta$ -hydroxyethyl acrylate and  $\beta$ -hydroxyethyl methacrylate), and acrylic acid or methacrylic acid alkyl esters (e.g., methyl acrylate, methyl methacrylate, ethyl acrylate, ethyl methacrylate, butyl acrylate, butyl methacrylate, 2-ethylhexyl acrylate, and 2-ethylhexyl methacrylate).

If required, conventionally known other components such as a polymerization inhibitor, a plasticizer, a pigment, a dye, a surfactant, a defoaming agent, and a coupling agent may also be incorporated into the composition of the invention.

The photosensitive resin composition of the present invention exhibits high sensitivity even when the composition has low concentration. Thus, when an low-concentration (e.g., about 3% in solid content) aqueous solution of the composition is subjected to photopolymerization, a hydrogel can be formed.

Into the photosensitive resin composition of the present invention, any of the functional components including a variety of drug ingredients, enzymes, bacterial cells, etc. may be incorporated. In this case, a photosensitive resin composition containing any of a variety of drug ingredients, enzymes, bacterial cells, etc. is photocured, whereby a hydrogel containing any of a variety of drug ingredients, enzymes, bacterial cells, etc. can be formed. Needless to say, after formation of a hydrogel from the photosensitive resin composition of the present invention, the hydrogel may be impregnated with any of a variety of drug ingredients, enzymes, bacterial cells, etc.

Similar to a conventional resist composition, the photosensitive resin composition of the present invention may be patterned. Thus, a photosensitive resin composition containing any of the functional components including a variety of drug ingredients, enzymes, bacterial cells, etc. or a hydrogel formed from the photosensitive resin composition of the present invention and impregnated with any of the functional components including a variety of drug ingredients, enzymes, bacterial cells, etc. may be patterned through photolithography.

The present invention will next be described in detail by way of examples, which should not be construed as limiting the invention thereto. Needless to say, a variety of photosensitive resin compositions obtained from the photosensitive resin and finding various uses fall within the

scope of the present invention.

<Example 1>

Poly(acrylic acid) (Aqualic AS-58, product of Nippon Shokubai Co., Ltd., weight average molecular weight of 800,000) (10 g) was dissolved in methanol (75 g) with heating. 4-Hydroxybutyl acrylate glycidyl ether (4HBAGE, product of Nippon Kasei Chemical Co., Ltd.) (1.6 g) and pyridine (1.1 g) serving as a catalyst for accelerating reaction were added to the above methanol solution, and the mixture was stirred on a 55°C-hot-water bath for 24 hours. Methanol was removed by elevating the bath temperature to 90°C while water was added dropwise to the mixture, followed by treating with ion-exchange resin (PK-216H, product of Mitsubishi Chemical Corporation), to thereby remove pyridine, whereby an aqueous solution of photosensitive resin (A) (non-volatile solid content: 13%) was produced. The acid value of photosensitive resin (A), as determined through titration with a 0.1M aqueous NaOH, was 630 mgKOH/g on a solid basis. To the 13% aqueous solution (100 g) of photosensitive resin (A), 1-[4-(2-hydroxyethoxy)-phenyl]-2-hydroxy-2-methyl-1-propan-1-one (IRGACURE-2959, product of Ciba Specialty Chemicals K.K.) (0.1 g) serving as a photopolymerization initiator was added, to thereby produce an aqueous solution of a photosensitive resin composition of interest.

The thus-produced aqueous photosensitive resin composition solution was diluted with water, to thereby prepare samples having solid contents shown in Table 1. Each



sample was placed in a test tube sealed with a stopper. The sample was irradiated with a UV ray having an illuminance of 250 mW/cm<sup>2</sup> emitted from a metal halide lamp UV radiator for four seconds. After completion of irradiation, the test tube was placed upright, and the stopper was removed. An iron ball (5.5 g) was placed on the surface of each sample, and hardenability of the samples was evaluated with comparison on the basis of the status (sinking or floating) of the iron ball.

[Table 1]

Solid content	2%	3%	4%	6%	8%	10%
Iron ball	sink	float	float	float	float	float

<Example 2>

The aqueous solution of photosensitive resin (A) synthesized in Example 1 was neutralized with sodium hydroxide, to thereby produce an aqueous solution having a non-volatile solid content of 10.4% (pH = 6.0). To the solution (100 g), 1-[4-(2-hydroxyethoxy)-phenyl]-2-hydroxy-2-methyl-1-propan-1-one (IRGACURE-2959, product of Ciba Specialty Chemicals K.K.) (0.08 g) serving as a photopolymerization initiator was added, to thereby produce an aqueous solution of a photosensitive resin composition.

The thus-produced aqueous photosensitive resin composition solution was diluted with water, to thereby prepare samples having solid contents shown in Table 2. Under the same conditions as employed in Example 1,

hardenability of the samples was evaluated with comparison on the basis of the status (sinking or floating) of the iron ball.

[Table 2]

Solid content	2%	3%	4%	6%	8%	10%
Iron ball	sink	float	float	float	float	float

<Comparative Example 1>

PVA-SbQ resin (SPP-H-13, product of Toyo Gosei Co., Ltd., polymerization degree of 1,700) was diluted with water, to thereby prepare samples having solid contents shown in Table 3. In a manner similar to that of Example 1, hardenability of the samples was evaluated.

[Table 3]

Solid content	2%	3%	4%	6%	8%	10%
Iron ball	sink	sink	sink	sink	float	float

As is clear from Tables 1 to 3, low-concentration samples (solid content: 3%) of Examples 1 and 2 formed uniform hydrogels having high gel strength and were able to maintain an iron ball on the gel surface. In contrast, the samples of Comparative Example 1 were able to maintain an iron ball on the sample surface, only when the solid content of the sample increased to 8%, which is a threshold concentration higher than that determined in the Examples.

## Industrial Applicability

The photosensitive resin composition of the present invention exhibits excellent storage stability and affinity, miscibility, or solubility with respect to a variety of compounds. In addition, the composition forms, at remarkably high-speed, a uniform hydrogel having high gel strength, even though the composition has a low concentration. Thus, the composition of the present invention is remarkably useful.